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FILE COVERS 1907 - 7 Jul 2003 VOL 139 ISS 2
FILE LAST UPDATED: 6 Jul 2003 (20030706/ED)

This file contains CAS Registry Numbers for easy and accurate substance identification.

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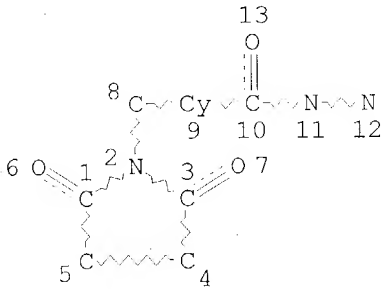
L1 STR




NODE ATTRIBUTES:
DEFAULT MLEVEL IS ATOM
DEFAULT ECLEVEL IS LIMITED

GRAPH ATTRIBUTES:
RING(S) ARE ISOLATED OR EMBEDDED
NUMBER OF NODES IS 13

STEREO ATTRIBUTES: NONE
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L4 13 SEA FILE=HCAPLUS ABB=ON PLU=ON L3

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L4 ANSWER 1 OF 13 HCAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 2002:298807 HCAPLUS
DOCUMENT NUMBER: 136:400166
TITLE: Constructing an adenocarcinoma vaccine: Immunization

of mice with synthetic KH-1 nonasaccharide stimulates anti-KH-1 and anti-Ley antibodies

AUTHOR(S): Ragupathi, Govindaswami; Deshpande, Prashant P.; Coltart, Don M.; Kim, Hyunjin M.; Williams, Lawrence J.; Danishefsky, Samuel J.; Livingston, Philip O.

CORPORATE SOURCE: Laboratory of Tumor Vaccinology, Department of Medicine, Memorial Sloan-Kettering Cancer Center, New York, NY, USA

SOURCE: International Journal of Cancer (2002), 99(2), 207-212
CODEN: IJCNAW; ISSN: 0020-7136

PUBLISHER: Wiley-Liss, Inc.

DOCUMENT TYPE: Journal

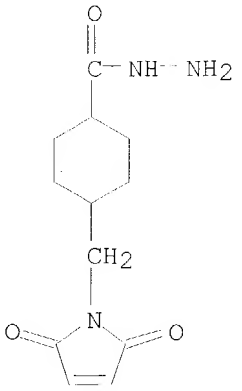
LANGUAGE: English

AB There is mounting evidence to suggest that immunization-based strategies can be used to mobilize the human immune system against specific carbohydrate antigens displayed on the surface of cancer cells. Following isolation and identification, such antigens can be administered as conjugate vaccines. The tumor-assocd. carbohydrate antigen KH-1 is 1 such antigen and may serve as a potential target for immunization against adenocarcinoma. However, a serious impediment to the application of a vaccine-based approach involving this antigen is that its availability from natural sources is severely limited. In order to overcome this limitation, the authors have developed an efficient total synthesis of this complex glycolipid. The authors have extended the synthesis to reach a structurally related analog in which the ceramide portion of KH-1 is replaced with an allyl substituent. These synthetic advances have led to the prepn. of 2 potential vaccine constructs, each based on the conjugation of the KH-1 nonasaccharide and the carrier protein keyhole limpet hemocyanin (KLH). In 1 construct (KH-1-Et-KLH), the nonasaccharide is conjugated to KLH via a simple Et linkage, while in the other (KH-1-MMCCH-KLH), conjugation is mediated by a 4-(4-N-maleimidomethyl)cyclohexane-1-carboxyl hydrazide (MMCCH) cross-linker. The authors report here the immunol. properties of these 2 constructs. Mice were immunized with either of the 2 KH-1-KLH vaccine candidates or the KH-1 ceramide, along with the immunol. adjuvant QS-21. Immunization with the ceramide served as a neg. control and, as expected, failed to stimulate the prodn. of antibodies against the KH-1 glycolipid. The construct in which the KH-1 nonasaccharide is linked to KLH via a simple alkyl chain stimulated significant quantities of IgM antibodies, whereas the construct linked to KLH by MMCCH induced high titers of both IgM and IgG antibodies. Inhibition data demonstrated that antibodies generated in response to immunization with the KH-1-KLH constructs recognize not only the KH-1 antigen but also the Lewisy (Ley) antigen, which, from a structural perspective, is similar to the 4 residues located at the non-reducing end of the KH-1 nonasaccharide. Thus, the KH-1-KLH constructs elicit an immune response that successfully targets 2 adenocarcinoma markers. As assessed by FACS anal., the antibodies raised were strongly reactive with the KH-1/Ley pos. cell line MCF-7 but not with KH-1 and Ley neg. melanoma cell lines. Based on the results of this study, a KH-1-KLH plus QS-21 vaccine is being prepd. for clin. evaluation.

IT **181148-00-5**
RL: BSU (Biological study, unclassified); BIOL (Biological study) (for conjugation of KH-1 nonasaccharide to keyhole limpet hemocyanin carrier)

RN 181148-00-5 HCAPLUS

CN Cyclohexanecarboxylic acid, 4-[(2,5-dihydro-2,5-dioxo-1H-pyrrol-1-yl)methyl]-, hydrazide (9CI) (CA INDEX NAME)



REFERENCE COUNT: 21 THERE ARE 21 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

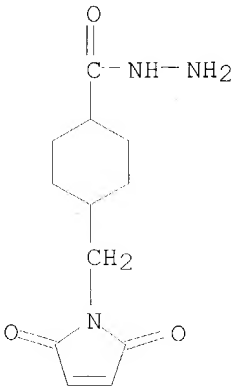
L4 ANSWER 2 OF 13 HCAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 2001:435302 HCAPLUS
DOCUMENT NUMBER: 135:41770
TITLE: Silanized nucleic acids for immobilization on glass and silicon surfaces
INVENTOR(S): Liang, Zicai; Kumar, Anil
PATENT ASSIGNEE(S): Karolinska Innovations Ab, Swed.
SOURCE: PCT Int. Appl., 29 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| WO 2001042501 | A1 | 20010614 | WO 2000-SE2446 | 20001206 |
| W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM | | | | |
| RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG | | | | |
| EP 1235937 | A1 | 20020904 | EP 2000-983641 | 20001206 |
| R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR | | | | |

PRIORITY APPLN. INFO.: SE 1999-4506 A 19991209
US 1999-170208P P 19991210
WO 2000-SE2446 W 20001206

AB A method for immobilization of nucleic acids onto glass and silicon surfaces is described, wherein said nucleic acids are immobilized onto unmodified glass and other silicon surfaces. A new class of modified nucleic acids, namely silanized nucleic acids, and methods of prepg. such modified nucleic acids, as well as a method for producing DNA chips of various d. with only end-attachment of DNA applied, are also described. Thus, 3 methods of silanizing nucleic acids are described. According to the first method, groups on the silanizing agent and the nucleic acid react to form a bond. In the second method, a coupling agent is used to form the bond. By the third method, linkages are formed with acrylic groups on the silanizing agent and the nucleic acid.

IT **174422-72-1**
RL: RCT (Reactant); RACT (Reactant or reagent)
(bifunctional crosslinker; silanized nucleic acids for immobilization on glass and silicon surfaces)
RN 174422-72-1 HCAPLUS
CN Cyclohexanecarboxylic acid, 4-[(2,5-dihydro-2,5-dioxo-1H-pyrrol-1-yl)methyl]-, hydrazide, monohydrochloride (9CI) (CA INDEX NAME)



● HCl

REFERENCE COUNT: 5 THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 3 OF 13 HCAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 2001:150972 HCAPLUS
DOCUMENT NUMBER: 135:13979
TITLE: In vitro and in vivo efficacy of acid-sensitive transferrin and albumin doxorubicin conjugates in a human xenograft panel and in the MDA-MB-435 mamma carcinoma model
AUTHOR(S): Kratz, Felix; Roth, Thomas; Fichiner, Iduna; Schumacher, Peter; Fiebig, Heinz H.; Unger, Clemens
CORPORATE SOURCE: Department of Medical Oncology, Clinical Research, Tumor Biology Center, Freiburg, 79106, Germany
SOURCE: Journal of Drug Targeting (2000), 8(5), 305-318
CODEN: JDTAEH; ISSN: 1061-186X
PUBLISHER: Harwood Academic Publishers
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Acid-sensitive transferrin and albumin conjugates with doxorubicin have recently been developed with the aim of circumventing the systemic toxicity and improving the therapeutic efficacy of this anticancer agent. The in vitro activity of two acid-sensitive transferrin and albumin doxorubicin conjugates and free doxorubicin was evaluated in twelve human tumor xenografts using a clonogenic assay. The inhibitory effects and the activity profile of the conjugates was, in general, comparable to that of doxorubicin (mean IC70-value for doxorubicin .apprxeq. 0.1 .mu.M and 0.1-0.4 .mu.M for the conjugates). Subsequently, the efficacy of an acid-sensitive transferrin and albumin doxorubicin conjugate, which both incorporated a phenylacetyl hydrazone bond as a predetd. breaking point, was evaluated in the xenograft mamma carcinoma model MDA-MB-435 in comparison to free doxorubicin (dose, i.v.: 2.times.4, 8 and 12 mg/kg). The conjugates showed significantly reduced toxicity (reduced lethality

and body wt. loss) with a concomitantly stable or slightly improved antitumor activity compared to free doxorubicin. At the dose of 12 mg/kg mortality was unacceptably high in the doxorubicin treated group (.apprxeq.80%); in contrast, no mortality was obsd. with the conjugate treated animals with body wt. loss < 10%. In a further expt., therapy with the acid-sensitive doxorubicin albumin conjugate at 3.times.12 mg/kg in the MDA-MB-435 model resulted in a significantly improved antitumor activity over free doxorubicin at its optimal dose of 2.times.8 mg/kg. In conclusion, acid-sensitive transferrin and albumin doxorubicin conjugates can be administered at higher doses than free doxorubicin in nude mice models with a concomitant improvement in antitumor activity. Interestingly, there is no pronounced difference between identically constructed transferrin and albumin doxorubicin conjugates with regard to in vitro or in vivo efficacy.

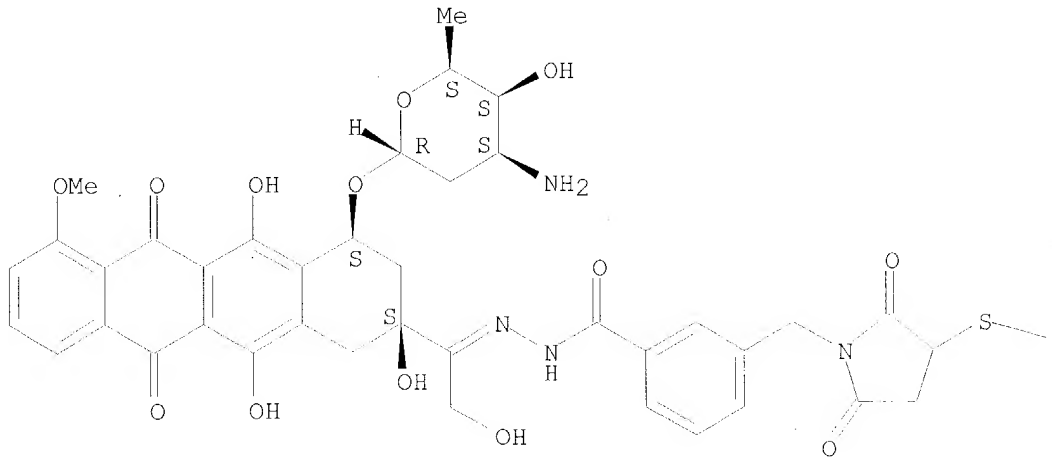
IT **342607-00-5D**, albumin and transferrin conjugates
RL: ADV (Adverse effect, including toxicity); BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(in vitro and in vivo efficacy of acid-sensitive transferrin and albumin doxorubicin conjugates in a human xenograft panel and in MDA-MB-435 mamma carcinoma model in relation to toxicity)

RN 342607-00-5 HCAPLUS

CN Benzoic acid, 3-[[3-[(4-amino-4-iminobutyl)thio]-2,5-dioxo-1-pyrrolidinyl]methyl]-, [1-[(2S,4S)-4-[(3-amino-2,3,6-trideoxy-.alpha.-L-lyxo-hexopyranosyl)oxy]-1,2,3,4,6,11-hexahydro-2,5,12-trihydroxy-7-methoxy-6,11-dioxo-2-naphthacenyl]-2-hydroxyethylidene]hydrazide, monohydrochloride (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry unknown.

PAGE 1-A

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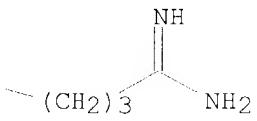


REFERENCE COUNT: 41 THERE ARE 41 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 4 OF 13 HCAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 2000:234766 HCAPLUS
DOCUMENT NUMBER: 133:43736
TITLE: Allylmalonamide as a bivalent linker: synthesis of biantennary GM3-saccharide-Keyhole limpet hemocyanin glycoconjugate and the immune response in mice
AUTHOR(S): Zou, Wei; Abraham, Mary; Gilbert, Michel; Wakarchuk, Warren W.; Jennings, Harold J.
CORPORATE SOURCE: Institute for Biological Sciences, National Research Council of Canada, Ottawa, ON, K1A OR6, Can.
SOURCE: Glycoconjugate Journal (2000), Volume Date 1999, 16(9), 507-515
CODEN: GLJOEW; ISSN: 0282-0080
PUBLISHER: Kluwer Academic Publishers
DOCUMENT TYPE: Journal
LANGUAGE: English
OTHER SOURCE(S): CASREACT 133:43736

AB A biantennary GM3-saccharide (sialyllactoside) deriv. was constructed using allylmalonic acid as a bivalent linker, both carboxylic acids of which were condensed with 3-aminopropyl lactoside prior to enzymic sialylation with a fusion enzyme. The av. ratios of saccharide to protein were obsd. to be 35 in KLH conjugate and 9-12 in HSA conjugates. The antisera obtained by immunizing mice with the biantennary sialyllactoside-KLH conjugate together with MPL adjuvant were analyzed by ELISA. Using several structurally related saccharide-HSA conjugates as screening antigens, it was concluded that anti-sialyllactoside antibodies, both IgG and IgM, were effectively raised. This was further supported by competitive inhibition expts. using lactoside, sialyllactoside and biantennary sialyllactoside as inhibitors.

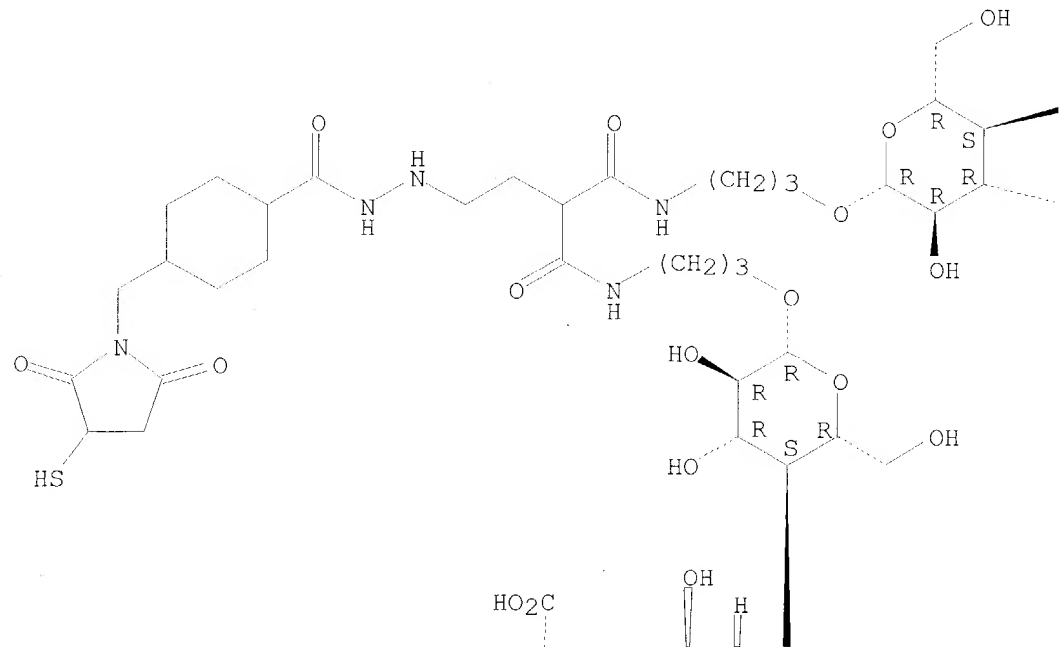
IT **274260-28-5DP**, human serum albumin and keyhole limpet hemocyanin bound
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)
(allylmalonamide as a bivalent linker synthesis of biantennary GM3-saccharide-keyhole limpet hemocyanin glycoconjugate and the immune response in mice)

RN 274260-28-5 HCAPLUS
CN Cyclohexanecarboxylic acid, 4-[(3-mercapto-2,5-dioxo-1-pyrrolidinyl)methyl]-, 2-[4-[[3-[[O-(N-acetyl-.alpha.-neuraminosyl)-(2.fwdarw.3)-O-.beta.-D-galactopyranosyl-(1.fwdarw.4)-.beta.-D-glucopyranosyl]oxy]propyl]amino]-3-[[[3-[[O-(N-acetyl-.alpha.-

neuraminosyl)-(2.fwdarw.3)-O-.beta.-D-galactopyranosyl-(1.fwdarw.4)-.beta.-D-glucopyranosyl]oxy]propyl]amino]carbonyl]-4-oxobutyl]hydrazide (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



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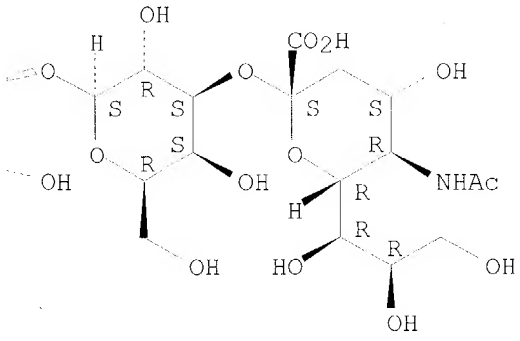

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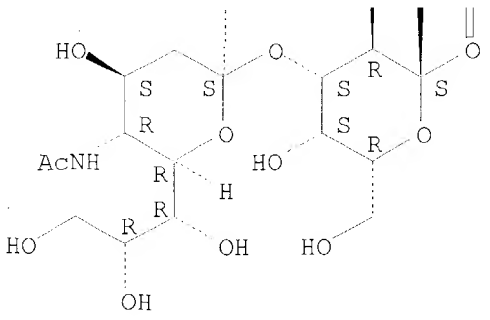


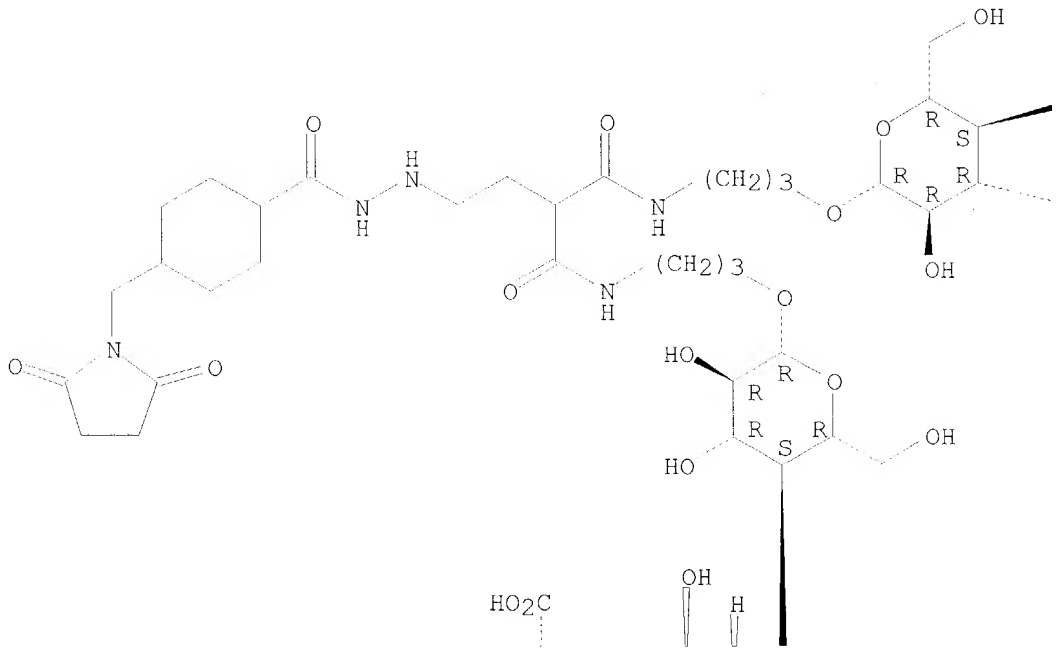
IT **274260-27-4P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(allylmalonamide as a bivalent linker synthesis of biantennary GM3-saccharide-keyhole limpet hemocyanin glycoconjugate and the immune response in mice)

RN 274260-27-4 HCAPLUS

CN Cyclohexanecarboxylic acid, 4-[(2,5-dioxo-1-pyrrolidinyl)methyl]-, 2-[4-[[3-[[O-(N-acetyl-.alpha.-neuraminosyl)-(2.fwdarw.3)-O-.beta.-D-galactopyranosyl-(1.fwdarw.4)-.beta.-D-glucopyranosyl]oxy]propyl]amino]-3-[[[3-[[O-(N-acetyl-.alpha.-neuraminosyl)-(2.fwdarw.3)-O-.beta.-D-galactopyranosyl-(1.fwdarw.4)-.beta.-D-glucopyranosyl]oxy]propyl]amino]carbonyl]-4-oxobutyl]hydrazide (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



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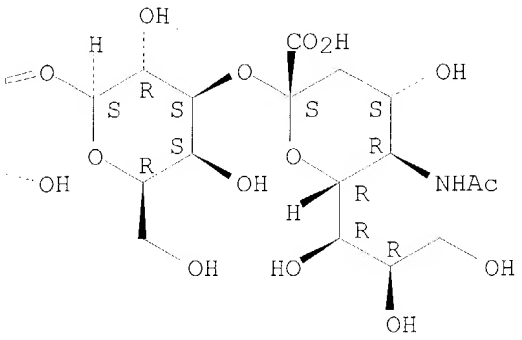

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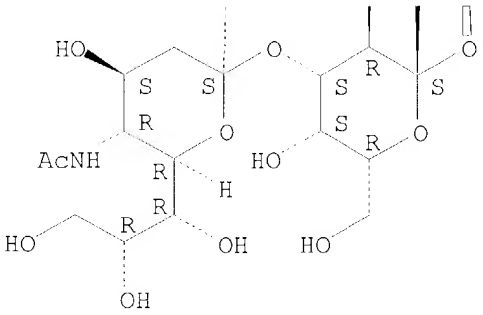

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L4 ANSWER 5 OF 13 HCAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 2000:68360 HCAPLUS
DOCUMENT NUMBER: 132:127703
TITLE: Water-soluble geldanamycin derivatives and methods for their production and cancer treatment
INVENTOR(S): Ho, David K.; Mandler, Raya; Alvarado-Lindner, Ada Belinda; Upadhyay, Kaye B. Dillah; Newman, David J.
PATENT ASSIGNEE(S): United States Dept. of Health and Human Services, USA
SOURCE: PCT Int. Appl., 60 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| WO 2000003737 | A2 | 20000127 | WO 1999-US16199 | 19990715 |
| WO 2000003737 | A3 | 20000420 | | |

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RW: GH, GM, KE, LS, MW, SD, SL, SZ, UG, ZW, AT, BE, CH, CY, DE, DK,

ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

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| CA 2338000 | AA | 20000127 | CA 1999-2338000 | 19990715 |
| AU 9951091 | A1 | 20000207 | AU 1999-51091 | 19990715 |
| EP 1098666 | A2 | 20010516 | EP 1999-935659 | 19990715 |
| R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO | | | | |
| JP 2002520369 | T2 | 20020709 | JP 2000-559871 | 19990715 |

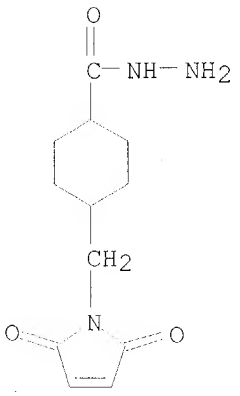
PRIORITY APPLN. INFO.: US 1998-93284P P 19980717
WO 1999-US16199 W 19990715

AB The present invention provides water-sol. drugs, in particular, water-sol. analogs of geldanamycin, and compns. comprising the same. This invention also provides a method of rendering water-insol. drugs sol. in water through derivatization with a bifunctional linking mol. and subsequent conjugation to a polar moiety through a thio ether. The present invention further provides a method of treating cancer in a mammal. Thus, 17-GMB-aminopropylaminogeldanamycin (prepn. given) was reacted with L-cysteine to give 17-cys-GMB-aminopropylaminogeldanamycin which was water sol. Growth inhibitory efficacy of sol. geldanamycin derivs. against cancer cells is shown.

IT **174422-72-1**
RL: RCT (Reactant); RACT (Reactant or reagent)
(water-sol. geldanamycin derivs. and methods for their prodn. and cancer treatment)

RN 174422-72-1 HCAPLUS

CN Cyclohexanecarboxylic acid, 4-[(2,5-dihydro-2,5-dioxo-1H-pyrrol-1-yl)methyl]-, hydrazide, monohydrochloride (9CI) (CA INDEX NAME)



● HCl

L4 ANSWER 6 OF 13 HCAPLUS COPYRIGHT 2003 ACS

ACCESSION NUMBER: 2000:9442 HCAPLUS
DOCUMENT NUMBER: 132:170955
TITLE: Acid-sensitive polyethylene glycol conjugates of doxorubicin: preparation, in vitro efficacy and intracellular distribution
AUTHOR(S): Rodrigues, Paula C. A.; Beyer, Ulrich; Schumacher, Peter; Roth, Thomas; Fiebig, Heinz H.; Unger, Clemens; Messori, Luigi; Orioli, PierLuigi; Paper, Dietrich H.; Mulhaupt, Rolf; Kratz, Felix
CORPORATE SOURCE: Department of Medical Oncology, Clinical Research, Tumor Biology Center, Freiburg, 79106, Germany

SOURCE: Bioorganic & Medicinal Chemistry (1999), 7(11), 2517-2524
CODEN: BMECEP; ISSN: 0968-0896
PUBLISHER: Elsevier Science Ltd.
DOCUMENT TYPE: Journal
LANGUAGE: English

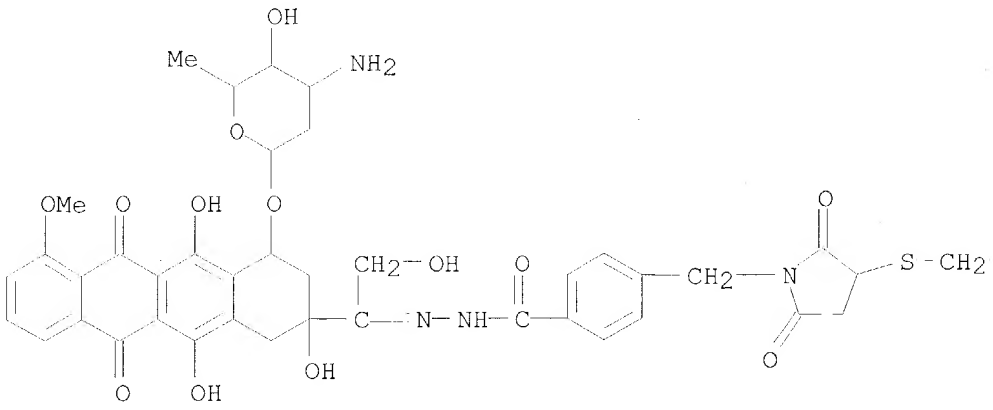
AB Coupling anticancer drugs to synthetic polymers is a promising approach of enhancing the antitumor efficacy and reducing the side-effects of these agents. Doxorubicin maleimide derivs. contg. an amide or acid-sensitive hydrazone linker were therefore coupled to .alpha.-methoxy-poly(ethylene glycol)-thiopropionic acid amide (MW 20000 Da), .alpha.,.omega.-bis-thiopropionic acid amide poly(ethylene glycol) (MW 20000 Da) or .alpha.-tert-butoxy-poly(ethylene glycol)-thiopropionic acid amide (MW 70000 Da) and the resulting polyethylene glycol (PEG) conjugates isolated through size-exclusion chromatog. The polymer drug derivs. were designed as to release doxorubicin inside the tumor cell by acid-cleavage of the hydrazone bond after uptake of the conjugate by endocytosis. The acid-sensitive PEG conjugates contg. the carboxylic hydrazone bonds exhibited in vitro activity against human BXF T24 bladder carcinoma and LXFL 529L lung cancer cells with IC70 values in the range 0.02-1.5 .mu.m (cell culture assay: propidium iodide fluorescence or colony forming assay). In contrast, PEG doxorubicin conjugates contg. an amide bond between the drug and the polymer showed no in vitro activity. Fluorescence microscopy studies in LXFL 529 lung cancer cells revealed that free doxorubicin accumulates in the cell nucleus whereas doxorubicin of the acid-sensitive PEG doxorubicin conjugates is primarily localized in the cytoplasm. Nevertheless, the acid-sensitive PEG doxorubicin conjugates retain their ability to bind to calf thymus DNA as shown by fluorescence and visible spectroscopy studies. Results regarding the effect of an acid-sensitive PEG conjugate of mol. wt. 20000 in the chorioallantoic membrane (CAM) assay indicate that this conjugate is significantly less embryotoxic than free doxorubicin although antiangiogenic effects were not obsd.

IT **258844-02-9P 258844-03-0P**
RL: ADV (Adverse effect, including toxicity); BAC (Biological activity or effector, except adverse); BPR (Biological process); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); PROC (Process); USES (Uses)
(acid-sensitive polyethylene glycol conjugates of doxorubicin: prepn., in vitro efficacy and intracellular distribution)

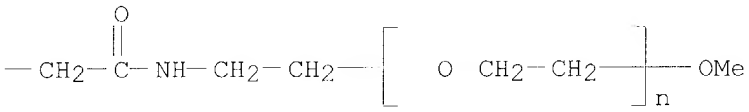
RN 258844-02-9 HCAPLUS

CN Poly(oxy-1,2-ethanediyl), .alpha.-[2-[[3-[[1-[[4-[[2-[1-[(2S,4S)-4-[(3-amino-2,3,6-trideoxy-.alpha.-L-lyxo-hexopyranosyl)oxy]-1,2,3,4,6,11-hexahydro-2,5,12-trihydroxy-7-methoxy-6,11-dioxo-2-naphthacenyl]-2-hydroxyethylidene]hydrazino]carbonyl]phenyl]methyl]-2,5-dioxo-3-pyrrolidinyl]thio]-1-oxopropyl]amino]ethyl]-.omega.-methoxy- (9CI) (CA INDEX NAME)

PAGE 1-A



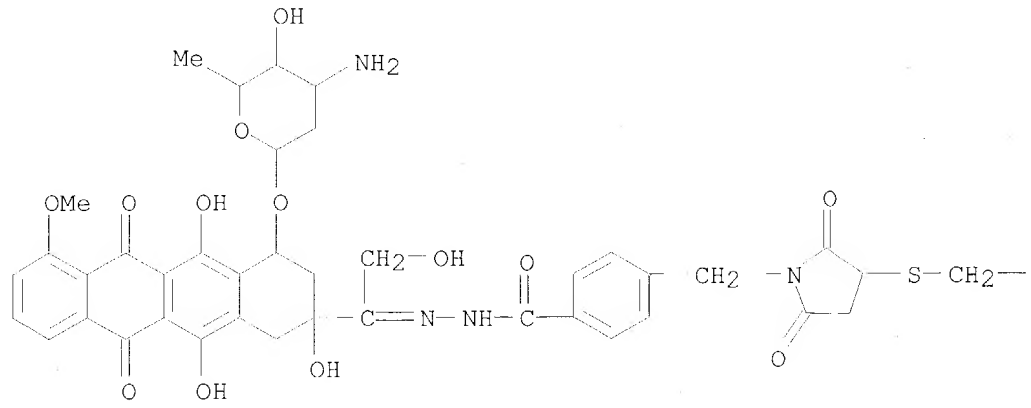
PAGE 1-B



RN 258844-03-0 HCAPLUS

CN Poly(oxy-1,2-ethanediyl), .alpha.-[2-[[3-[[1-[[4-[[2-[1-[(2S,4S)-4-[(3-amino-2,3,6-trideoxy-.alpha.-L-lyxo-hexopyranosyl)oxy]-1,2,3,4,6,11-hexahydro-2,5,12-trihydroxy-7-methoxy-6,11-dioxo-2-naphthacenyl]-2-hydroxyethylidene]hydrazino]carbonyl]phenyl]methyl]-2,5-dioxo-3-pyrrolidinyl]thio]-1-oxopropyl]amino]ethyl]-.omega.-[2-[[3-[[1-[[4-[[2-[1-[(2S,4S)-4-[(3-amino-2,3,6-trideoxy-.alpha.-L-lyxo-hexopyranosyl)oxy]-1,2,3,4,6,11-hexahydro-2,5,12-trihydroxy-7-methoxy-6,11-dioxo-2-naphthacenyl]-2-hydroxyethylidene]hydrazino]carbonyl]phenyl]methyl]-2,5-dioxo-3-pyrrolidinyl]thio]-1-oxopropyl]amino]ethoxy]- (9CI) (CA INDEX NAME)

PAGE 1-A



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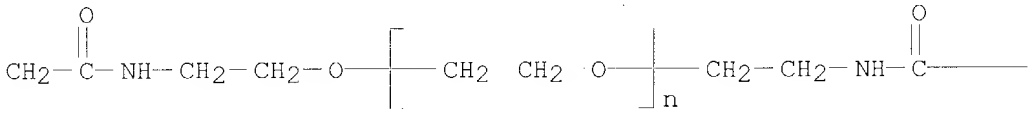
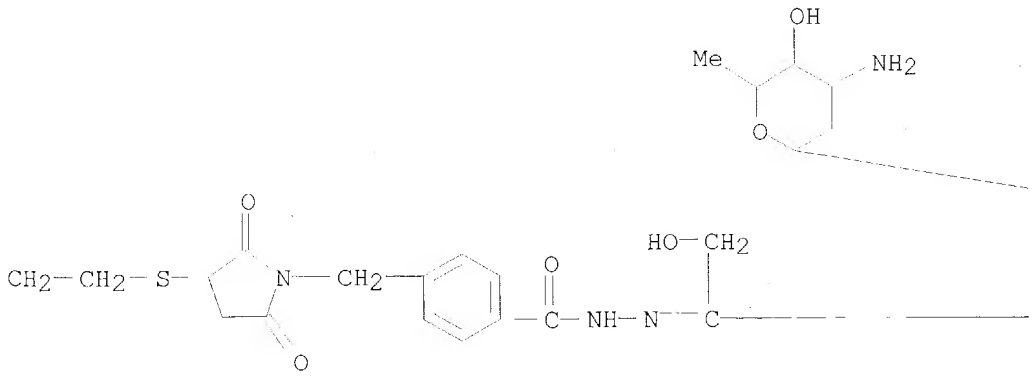


PAGE 1-C



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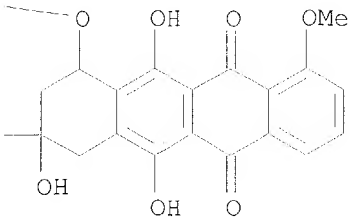



REFERENCE COUNT: 18 THERE ARE 18 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 7 OF 13 HCAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 1999:332718 HCAPLUS
DOCUMENT NUMBER: 131:143211
TITLE: Vaccines prepared with sialyl-Tn and sialyl-Tn trimers using the 4-(4-maleimidomethyl)cyclohexane-1-carboxyl hydrazide linker group result in optimal antibody titers against ovine submaxillary mucin and sialyl-Tn-positive tumor cells
AUTHOR(S): Ragupathi, Govindaswami; Howard, Lisa; Cappello, Sarah; Koganty, R. Rao; Qiu, Dongxu; Longenecker, B. Michael; Reddish, Mark A.; Lloyd, Kenneth O.; Livingston, Philip O.
CORPORATE SOURCE: Clinical Immunology Service, Department of Medicine, Memorial Sloan-Kettering Cancer Center, New York, NY, 10021, USA
SOURCE: Cancer Immunology Immunotherapy (1999), 48(1), 1-8
CODEN: CIIMDN; ISSN: 0340-7004
PUBLISHER: Springer-Verlag
DOCUMENT TYPE: Journal
LANGUAGE: English

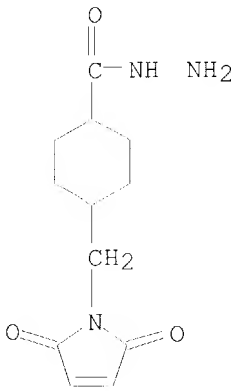
AB Sialyl-Tn (STn) is an O-serine- or O-threonine-linked disaccharide [NeuAc.alpha.(2.fwdarw.6)GalNAc.alpha.-O-Ser/Thr] expressed on mucins of most types of adenocarcinoma as single STn or clustered STn [STn(c)] epitopes. Though STn is expressed on some normal tissues it is relatively tumor-specific, esp. in the clustered conformation. Clin. trials with STn-keyhole limpet hemocyanin (KLH) conjugate vaccines, prepd. using reductive amination with a two-carbon linker group, have resulted in high titers against STn but lower titers against natural forms of STn (ovine submaxillary mucin, or tumor cells). To obtain antibodies of more appropriate specificity, the authors attempted to prep. STn(c)-KLH conjugates to establish their immunogenicity in mice in prepn. for clin. trials; however, conjugation efficiency was poor when the same 2-carbon linker was used, presumably because of steric hindrance. STn-KLH and STn(c)-KLH conjugates were prepd. using the regular 2-carbon or the recently developed more efficient longer heterobifunctional 4-(4-maleimidomethyl)cyclohexane-1-carboxyl hydrazide (MMCCH) linkers, and the resulting immunogenicities in mice were compared. The highest titers against STn were seen with the STn-KLH conjugate with the 2-carbon linker, and the highest titers against STn(c) were seen with STn(c)-KLH with the MMCCH linker. Conjugation with MMCCH resulted in the highest conjugation efficiency (yield) and the highest titers against ovine submaxillary mucin

and STn-pos. tumor cells, and is the method of choice for the prepn. of STn(c) vaccine for clin. trials.

IT **181148-00-5**
RL: BSU (Biological study, unclassified); BIOL (Biological study) (linker; vaccines prepd. with sialyl-Tn and sialyl-Tn trimers using linker group result in optimal antibody titers against ovine mucin and sialyl-Tn-pos. tumor cells)

RN 181148-00-5 HCAPLUS

CN Cyclohexanecarboxylic acid, 4-[(2,5-dihydro-2,5-dioxo-1H-pyrrol-1-yl)methyl]-, hydrazide (9CI) (CA INDEX NAME)



REFERENCE COUNT: 47 THERE ARE 47 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 8 OF 13 HCAPLUS COPYRIGHT 2003 ACS

ACCESSION NUMBER: 1998:235657 HCAPLUS
DOCUMENT NUMBER: 129:3682
TITLE: A novel and efficient method for synthetic carbohydrate conjugate vaccine preparation: synthesis of sialyl Tn-KLH conjugate using a 4-(4-N-maleimidomethyl) cyclohexane-1-carboxyl hydrazide (MMCCH) linker arm
AUTHOR(S): Ragupathi, Govindaswami; Koganty, R. Rao; Qiu, Dongxu; Lloyd, Kenneth O.; Livingston, Philip O.
CORPORATE SOURCE: Clinical Immunology Service, Memorial Hospital, New York, NY, 10021, USA
SOURCE: Glycoconjugate Journal (1998), 15(3), 217-221
CODEN: GLJOEW; ISSN: 0282-0080
PUBLISHER: Chapman & Hall
DOCUMENT TYPE: Journal
LANGUAGE: English

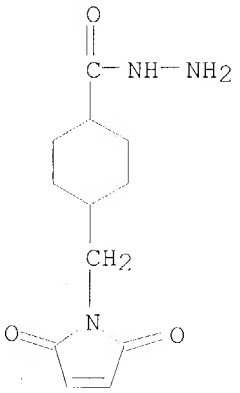
AB STn (NeuAc.alpha.2.fwdarw.6GalNAc.alpha.-O-Ser/Thr) is a carbohydrate epitope overexpressed in various human carcinomas. Clin. trials are underway using synthetic STn or STn trimeric glycopeptides [STn, cluster; STn(c)] conjugated with keyhole limpet hemocyanin (KLH) as active specific immunotherapy for these cancers. These vaccines have been prepd. by conjugating a crotyl Et amide deriv. of STn or STn(c) to KLH by direct reductive amination after ozonolysis. In the case of STn(c) the conjugation efficiency and the resulting epitope ratios were low. This may be due to steric hindrance of the short spacer arm. To overcome these difficulties, without resynthesis, the STn(c) glycopeptide was modified by attachment of an MMCCH (4-(4-N-maleimidomethyl) cyclohexane-1-carboxyl hydrazide) spacer arm to the aldehyde deriv., and then conjugated with thiolated KLH. This method gave a higher epitope ratio and yield than the direct method. The STn(c)-MMCCH-KLH conjugate induced high titer antibodies in mice against STn(c). This method may be generally

applicable for large synthetic oligosaccharides.

IT **174422-72-1**
RL: RCT (Reactant); RACT (Reactant or reagent)
(as spacer arm in sialyl Tn carcinoma vaccine)

RN 174422-72-1 HCAPLUS

CN Cyclohexanecarboxylic acid, 4-[(2,5-dihydro-2,5-dioxo-1H-pyrrol-1-yl)methyl]-, hydrazide, monohydrochloride (9CI) (CA INDEX NAME)



● HCl

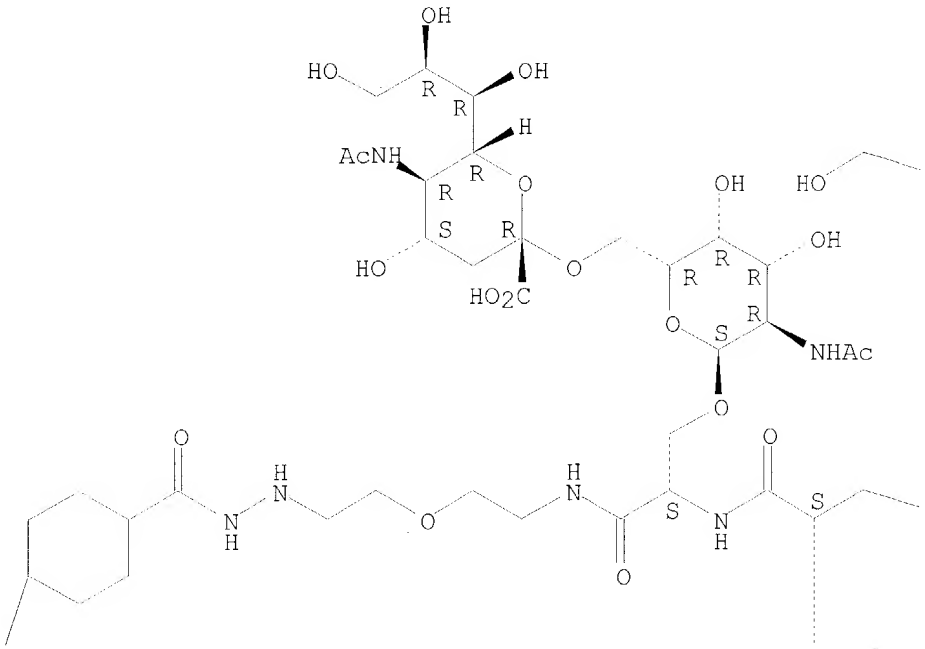
IT **207503-53-5DP**, keyhole limpet hemocyanin conjugates
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(immunogenicity of in carcinoma vaccine)

RN 207503-53-5 HCAPLUS

CN L-Serinamide, N-acetyl-O-[2-(acetylamino)-6-O-(N-acetyl-.alpha.-neuraminosyl)-2-deoxy-.alpha.-D-galactopyranosyl]-L-seryl-O-[2-(acetylamino)-6-O-(N-acetyl-.alpha.-neuraminosyl)-2-deoxy-.alpha.-D-galactopyranosyl]-L-seryl-O-[2-(acetylamino)-6-O-(N-acetyl-.alpha.-neuraminosyl)-2-deoxy-.alpha.-D-galactopyranosyl]-N-[2-[2-[2-[[4-[(2,5-dihydro-2,5-dioxo-1H-pyrrol-1-yl)methyl]cyclohexyl]carbonyl]hydrazino]ethoxy]ethyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



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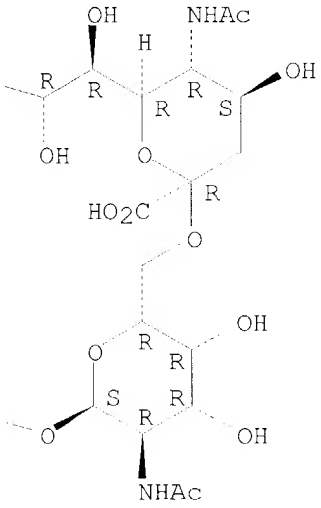

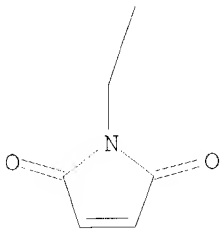

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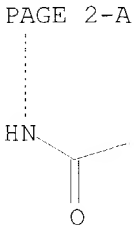
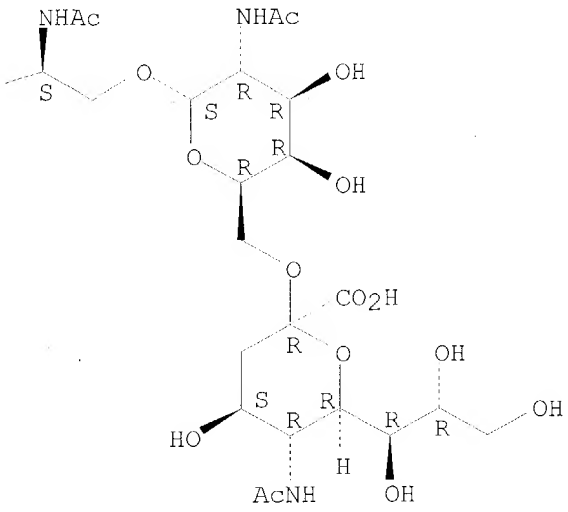


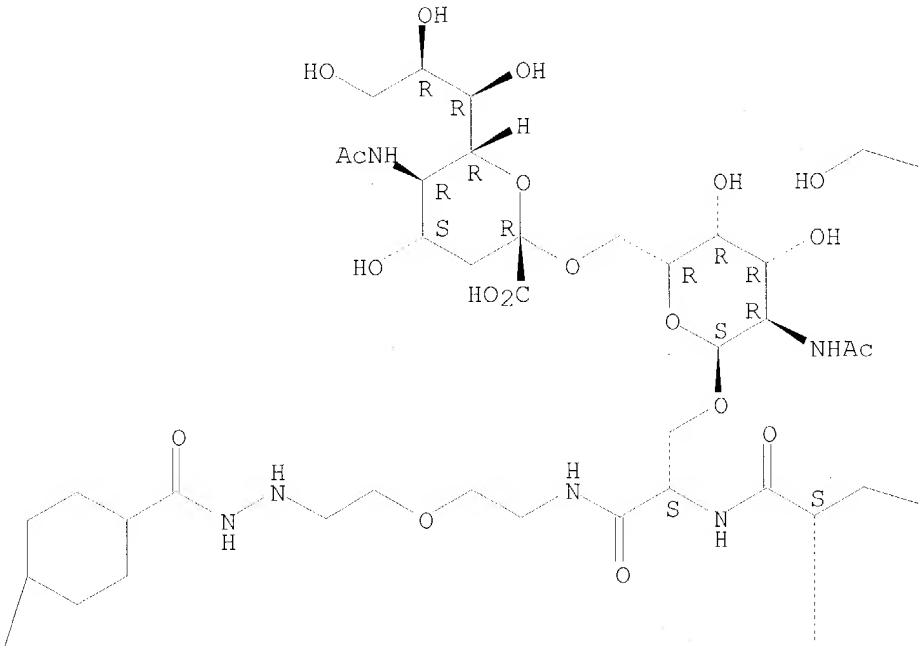
PAGE 2-B



IT **207503-53-5P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(prepn. of and conjugation to keyhole limpet hemocyanin)
RN 207503-53-5 HCAPLUS
CN L-Serinamide, N-acetyl-O-[2-(acetylamino)-6-O-(N-acetyl-.alpha.-neuraminosyl)-2-deoxy-.alpha.-D-galactopyranosyl]-L-seryl-O-[2-(acetylamino)-6-O-(N-acetyl-.alpha.-neuraminosyl)-2-deoxy-.alpha.-D-galactopyranosyl]-L-seryl-O-[2-(acetylamino)-6-O-(N-acetyl-.alpha.-neuraminosyl)-2-deoxy-.alpha.-D-galactopyranosyl]-N-[2-[2-[2-[[4-[(2,5-dihydro-2,5-dioxo-1H-pyrrol-1-yl)methyl]cyclohexyl]carbonyl]hydrazino]ethoxy]ethyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



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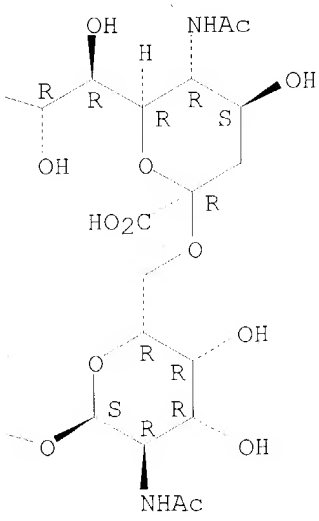

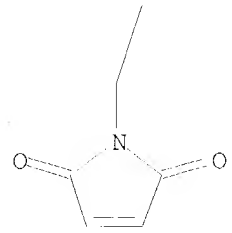

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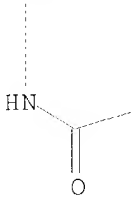

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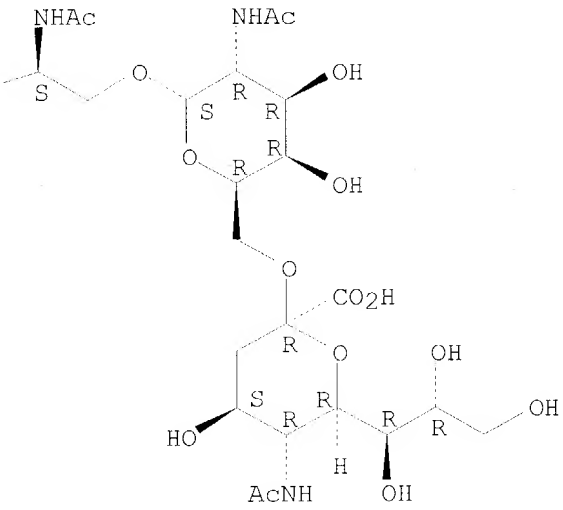


REFERENCE COUNT: 25 THERE ARE 25 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

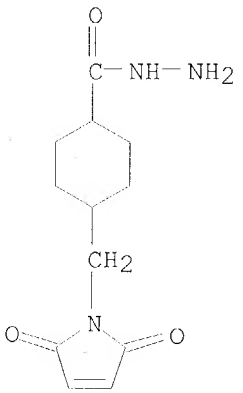
L4 ANSWER 9 OF 13 HCAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 1998:129059 HCAPLUS
DOCUMENT NUMBER: 128:203897
TITLE: Immunogenicity of synthetic conjugates of Lewisy oligosaccharide with proteins in mice: towards the design of anticancer vaccines
AUTHOR(S): Kudryashov, Valery; Kim, Hyunjin M.; Ragupathi, Govindaswami; Danishefsky, Samuel J.; Livingston, Philip O.; Lloyd, Kenneth O.
CORPORATE SOURCE: Immunology Program, Memorial Sloan-Kettering Cancer Center, New York, NY, 10021, USA
SOURCE: Cancer Immunology Immunotherapy (1998), 45(6), 281-286
CODEN: CIIMDN; ISSN: 0340-7004
PUBLISHER: Springer-Verlag
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Many human carcinomas overexpress the Lewisy (Ley) blood-group epitope [Fuc.alpha.1 .fwdarw. 2Gal.beta.1 .fwdarw. 4 (Fuc.alpha.1 .fwdarw. 3)GlcNAc.beta.1 .fwdarw. 3Gal-]. With a view to developing Ley based vaccines we have examd. the immunogenicity of Ley-protein conjugates in mice. Ley pentasaccharide was synthesized as its allyl glycoside and coupled to keyhole limpet hemocyanin (KLH) by reductive amination or by a novel method utilizing a maleido-derivatized alkyl carboxyhydrazide as a bridging group to 2-iminothiolane-derivatized KLH. Ley oligosaccharide

was also coupled to bovine serum albumin by reductive amination. Immunization of groups of mice with the three conjugates, together with the immunol. adjuvant QS21, showed that Ley oligosaccharide directly coupled to KLH was the most efficient conjugate for eliciting IgG and IgM antibody responses to naturally occurring forms of Ley epitopes carried on mucins and glycolipids. These antibodies were also reactive with and cytotoxic to a human breast cancer cell line expressing Ley (MCF-7). These expts. suggest that Ley-KLH antigen and QS21 adjuvant could be considered as an immunogenic therapeutic vaccine in carcinoma patients.

IT **181148-00-5P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(Ley pentasaccharide coupling with)

RN 181148-00-5 HCAPLUS

CN Cyclohexanecarboxylic acid, 4-[(2,5-dihydro-2,5-dioxo-1H-pyrrol-1-yl)methyl]-, hydrazide (9CI) (CA INDEX NAME)



REFERENCE COUNT: 36 THERE ARE 36 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 10 OF 13 HCAPLUS COPYRIGHT 2003 ACS

ACCESSION NUMBER: 1998:43704 HCAPLUS

DOCUMENT NUMBER: 128:152804

TITLE: Antibody immobilization using heterobifunctional crosslinkers

AUTHOR(S): Shriver-Lake, Lisa C.; Donner, Brian; Edelstein, Rebecca; Breslin, Kristen; Bhatia, Suresh K.; Ligler, France S.

CORPORATE SOURCE: Center for Bio/Molecular Science and Engineering, Naval Research Laboratory, Washington, DC, 20375-5348, USA

SOURCE: Biosensors & Bioelectronics (1997), 12(11), 1101-1106
CODEN: BBIOE4; ISSN: 0956-5663

PUBLISHER: Elsevier Science Ltd.

DOCUMENT TYPE: Journal

LANGUAGE: English

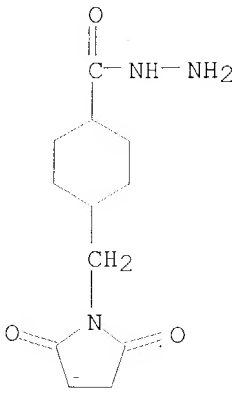
AB Covalent attachment of functional proteins to a solid support is important for biosensors. One method employs thiol-terminal silanes and hetero-bifunctional crosslinkers such as N-succinimidyl 4-maleimidobutyrate (GMBS) to immobilize proteins through amino groups onto glass, silica, silicon or platinum surfaces. In this report, several heterobifunctional crosslinkers are compared to GMBS for their ability to immobilize active antibodies onto glass cover slips at a high d. Antibodies were immobilized at densities of 74-220 ng/cm2 with high levels of specific antigen binding. Carbohydrate-reactive crosslinkers were also compared to GMBS using a fiber optic biosensor to detect

fluorescently-labeled antigen. At the concns. tested, the antibodies immobilized with carbohydrate-reactive crosslinkers bound more antigen than GMBS immobilized antibodies as indicated by the fluorescence signal.

IT **174422-72-1**
RL: RCT (Reactant); RACT (Reactant or reagent)
(amine-reactive and carbohydrate-reactive heterobifunctional crosslinkers in immobilization of antibodies)

RN 174422-72-1 HCAPLUS

CN Cyclohexanecarboxylic acid, 4-[(2,5-dihydro-2,5-dioxo-1H-pyrrol-1-yl)methyl]-, hydrazide, monohydrochloride (9CI) (CA INDEX NAME)



● HCl

REFERENCE COUNT: 10 THERE ARE 10 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 11 OF 13 HCAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 1996:563494 HCAPLUS
DOCUMENT NUMBER: 125:189998
TITLE: Immunoenzymic conjugate and its preparation and uses
INVENTOR(S): Cucurou, Christophe; Cognet, Gilles; Gadelle, Stephane; Le Sager, Carine
PATENT ASSIGNEE(S): Pasteur Sanofi Diagnostics, Fr.
SOURCE: PCT Int. Appl., 34 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: French
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
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| WO 9623226 | A1 | 19960801 | WO 1996-FR113 | 19960123 |
| W: AL, AM, AT, AU, AZ, BB, BG, BR, BY, CA, CH, CN, CZ, DE, DK, EE, ES, FI, GB, GE, HU, IS, JP, KE, KG, KP, KR, KZ, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI | | | | |
| RW: KE, LS, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE | | | | |
| FR 2729760 | A1 | 19960726 | FR 1995-735 | 19950123 |
| FR 2729760 | B1 | 19970814 | | |
| FR 2734365 | A1 | 19961122 | FR 1995-5939 | 19950518 |
| FR 2734365 | B1 | 19990409 | | |

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| CA 2184636 | AA | 19960801 | CA 1996-2184636 | 19960123 |
| AU 9646260 | A1 | 19960814 | AU 1996-46260 | 19960123 |
| AU 707172 | B2 | 19990701 | | |
| EP 752102 | A1 | 19970108 | EP 1996-901840 | 19960123 |
| EP 752102 | B1 | 20001115 | | |
| R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, MC, NL, PT, SE | | | | |
| ZA 9600504 | A | 19970723 | ZA 1996-504 | 19960123 |
| JP 09511067 | T2 | 19971104 | JP 1996-522674 | 19960123 |
| IL 116863 | A1 | 20000217 | IL 1996-116863 | 19960123 |
| AT 197645 | E | 20001215 | AT 1996-901840 | 19960123 |
| ES 2153090 | T3 | 20010216 | ES 1996-901840 | 19960123 |
| US 6027874 | A | 20000222 | US 1996-714110 | 19961122 |

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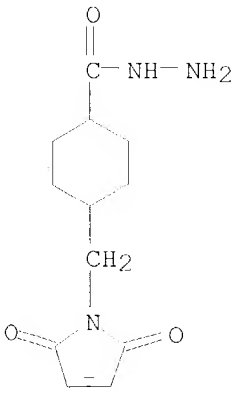
|---|---|---|---|
| PRIORITY APPLN. INFO.: | FR 1995-735 | A | 19950123 |
| | FR 1995-5939 | A | 19950518 |
| | WO 1996-FR113 | W | 19960123 |

AB An immunoenzymic conjugate is disclosed for, e.g, the diagnosis of virus infections, that consists of copolymeric glycosylated labeling enzymes (e.g., alk. phosphatase or peroxidase) conjugated with substances having immunol. activity, e.g., HIV1 peptide, HIV2 peptide, hepatitis C virus peptide, monoclonal antibody against HIV1, or antibody against hepatitis B surface antigen. The labeling enzyme mols. are copolymd. via their oxidized carbohydrates, and the enzyme copolymer is obtained by using a diamine, e.g., 1,4-phenylenediamine, or different heterobifunctional reagents, e.g., 2-mercaptoethylamine, 3-(2-pyridyldithio)propionyl hydrazide, etc. The enzyme copolymer is coupled to the immunol. substance by using a homo- or heterobifunctional reagent, e.g., bis(sulfosuccinimidyl)suberate, sulfosuccinimidyl-4-(N-maleimidomethyl)cyclohexane-1-carboxylate, or N-succinimidyl-3-(2-pyridyldithio)propionate. The use of such conjugates in diagnostic kits are also disclosed. Examples are given of the prepn. of conjugates of alk. phosphatase or peroxidase with a peptide from glycoprotein gp41 of HIV1, of a conjugate of peroxidase with monoclonal antibody against HIV1, of a conjugate of peroxidase with antibody against hepatitis B surface antigen, etc., and of their use in immunoassays for detection of the resp. antigens or antibodies.

IT **181148-00-5**
RL: ARG (Analytical reagent use); RCT (Reactant); ANST (Analytical study); RACT (Reactant or reagent); USES (Uses)
(enzyme polymer conjugates prepn. and use in immunoassays)

RN 181148-00-5 HCAPLUS

CN Cyclohexanecarboxylic acid, 4-[(2,5-dihydro-2,5-dioxo-1H-pyrrol-1-yl)methyl]-, hydrazide (9CI) (CA INDEX NAME)



L4 ANSWER 12 OF 13 HCAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 1995:978844 HCAPLUS

DOCUMENT NUMBER: 124:212048
TITLE: Erythropoietin with increased biological activity
INVENTOR(S): Sytokowski, Arthur J.
PATENT ASSIGNEE(S): New England Deaconess Hospital, USA
SOURCE: PCT Int. Appl., 41 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 3
PATENT INFORMATION:

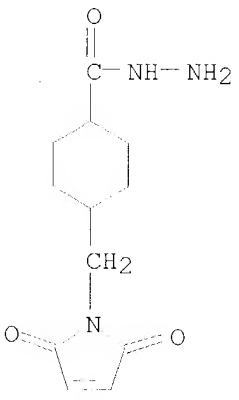
| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| WO 9525746 | A1 | 19950928 | WO 1995-US3242 | 19950315 |
| RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE | | | | |
| US 5580853 | A | 19961203 | US 1994-216259 | 19940322 |
| EP 751959 | A1 | 19970108 | EP 1995-912917 | 19950315 |
| EP 751959 | B1 | 20000105 | | |
| R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, MC, NL, PT, SE | | | | |
| AT 188486 | E | 20000115 | AT 1995-912917 | 19950315 |
| ES 2143620 | T3 | 20000516 | ES 1995-912917 | 19950315 |

PRIORITY APPLN. INFO.: US 1994-216259 A 19940322
WO 1995-US3242 W 19950315

AB Modified polypeptides with increased biol. activity exhibited as either increased potency or prolonged circulating half-life are prepd. by crosslinking their chains through cleavable disulfide groups. Thus, human erythropoietin was derivatized with a SPDP homolog and reduced with DTT to expose .gtoreq.1 SH group. A 2nd portion of native erythropoietin was derivatized with SMCC and mixed with the SH group-contg. erythropoietin to produce erythropoietin dimers and trimers. The dimeric erythropoietin showed increased biol. activity and had an in vivo half-life of >24 h, compared to 7 h for native erythropoietin.

IT **174422-72-1**
RL: RCT (Reactant); RACT (Reactant or reagent)
(crosslinked erythropoietin with increased biol. activity)

RN 174422-72-1 HCAPLUS
CN Cyclohexanecarboxylic acid, 4-[(2,5-dihydro-2,5-dioxo-1H-pyrrol-1-yl)methyl]-, hydrazide, monohydrochloride (9CI) (CA INDEX NAME)



● HCl

L4 ANSWER 13 OF 13 HCAPLUS COPYRIGHT 2003 ACS

ACCESSION NUMBER: 1990:548405 HCAPLUS
DOCUMENT NUMBER: 113:148405
TITLE: Targeting substance-diagnostic/therapeutic agent conjugates having Schiff base or hydrazone linkages, their use, and slow-release carrier-drug pharmaceuticals containing them
INVENTOR(S): Sivam, Gowsala P.; Reed, Michael W.; Srinivasan, Ananthachari; Morgan, A. Charles, Jr.; Brixner, Diana I.; Vrudhula, Vivekananda M.; Comezoglu, F. Taha
PATENT ASSIGNEE(S): NeoRx Corp., USA
SOURCE: PCT Int. Appl., 51 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| WO 9003401 | A1 | 19900405 | WO 1989-US4267 | 19890929 |
| W: JP | | | | |
| RW: AT, BE, CH, DE, FR, GB, IT, LU, NL, SE | | | | |
| EP 434765 | A1 | 19910703 | EP 1989-911718 | 19890929 |
| EP 434765 | B1 | 19951108 | | |
| R: AT, BE, CH, DE, FR, GB, IT, LI, LU, NL, SE | | | | |
| US 5066789 | A | 19911119 | US 1989-415154 | 19890929 |
| JP 04504248 | T2 | 19920730 | JP 1989-510891 | 19890929 |
| CA 2000039 | AA | 19900331 | CA 1989-2000039 | 19891002 |
| US 5633351 | A | 19970527 | US 1994-332045 | 19941101 |
| US 5521290 | A | 19960528 | US 1994-342789 | 19941121 |

PRIORITY APPLN. INFO.:
US 1988-252298 19880930
US 1989-415154 19890929
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US 1990-621709 19901204
US 1991-714806 19910613
US 1992-987535 19921207
US 1993-13484 19930201

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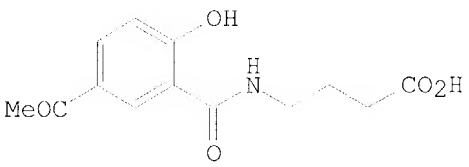



II

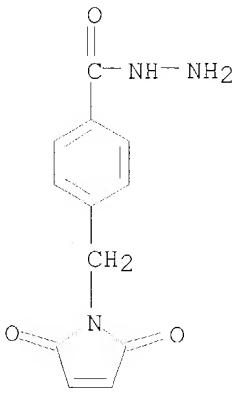
AB The title conjugates comprise e.g. TS-(L1)nC(O)NHN:C(R)(L2)n'-agent (TS is a targeting substance; L1 and L2 are heterobifunctional linkers; n, n' = 0, 1; R = H, alkyl, aryl, alicyclic; agent is a diagnostic or therapeutic agent or chelating agent for binding small therapeutic or diagnostic mols.). Slow-release carrier-drug pharmaceuticals incorporating the conjugates of the invention are described. Thus, tautomeric verrucarin A 2'-hemisuccinoylhydrazide (I) was prepd. from reacting the corresponding succinoylsuccinimidate (prepn. given) with H2NNH2. I was then reacted with the conjugate of monoclonal antibody NR-LU-10 and an N-hydroxysuccinimide ester of linker II. The resulting conjugate contained 4.4 verrucarin A mols./antibody mol. and displayed 1 log less cytotoxicity than verrucarin A itself.

IT **129506-88-3**
RL: ANST (Analytical study)

(in conjugate with diagnostic/therapeutic agent and targeting substance and Schiff base or hydrazone linkage)

RN 129506-88-3 HCAPLUS

CN Benzoic acid, 4-[(2,5-dihydro-2,5-dioxo-1H-pyrrol-1-yl)methyl]-, hydrazide (9CI) (CA INDEX NAME)



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USE IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT.
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FILE COVERS 1907-1966
FILE LAST UPDATED:  01 May 1997 (19970501/UP)

  This file contains CAS Registry Numbers for easy and accurate
  substance identification.  Title keywords, authors, patent
  assignees, and patent information, e.g., patent numbers, are
  now searchable from 1907-1966.  TIFF images of CA abstracts
  printed between 1907-1966 are available in the PAGE
  display formats.

  This file supports REGistRY for direct browsing and searching of
  all substance data from the REGISTRY file.  Enter HELP FIRST for
  more information.

=>
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=> d stat que l5 nos
L1               STR
L3            10 SEA FILE=REGISTRY SSS FUL L1
L5             0 SEA FILE=CAOLD ABB=ON  PLU=ON  L3


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PLEASE SEE "HELP USAGETERMS" FOR DETAILS.
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Property values tagged with IC are from the ZIC/VINITI data file provided by InfoChem.

STRUCTURE FILE UPDATES: 6 JUL 2003 HIGHEST RN 543672-54-4
DICTIONARY FILE UPDATES: 6 JUL 2003 HIGHEST RN 543672-54-4

TSCA INFORMATION NOW CURRENT THROUGH JANUARY 6, 2003

Please note that search-term pricing does apply when conducting SmartSELECT searches.

Crossover limits have been increased. See HELP CROSSOVER for details.

Experimental and calculated property data are now available. See HELP PROPERTIES for more information. See STNote 27, Searching Properties in the CAS Registry File, for complete details:
http://www.cas.org/ONLINE/STN/STNOTES/stnotes27.pdf

=>
=>

=> d ide can l3 1-10

L3 ANSWER 1 OF 10 REGISTRY COPYRIGHT 2003 ACS
RN 359436-59-2 REGISTRY
CN Cyclohexanecarboxylic acid, 4-[(2,5-dihydro-2,5-dioxo-1H-pyrrol-1-yl)methyl]-, hydrazide, mono(trifluoroacetate) (9CI) (CA INDEX NAME)
MF C12 H17 N3 O3 . C2 H F3 O2
SR CAS Registry Services
LC STN Files: CHEMCATS

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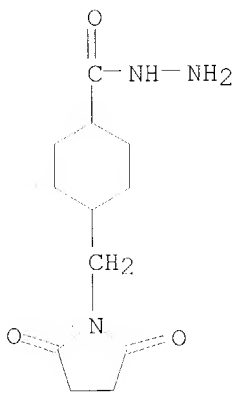
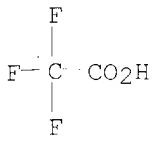
CRN 181148-00-5
CMF C12 H17 N3 O3



CM 2

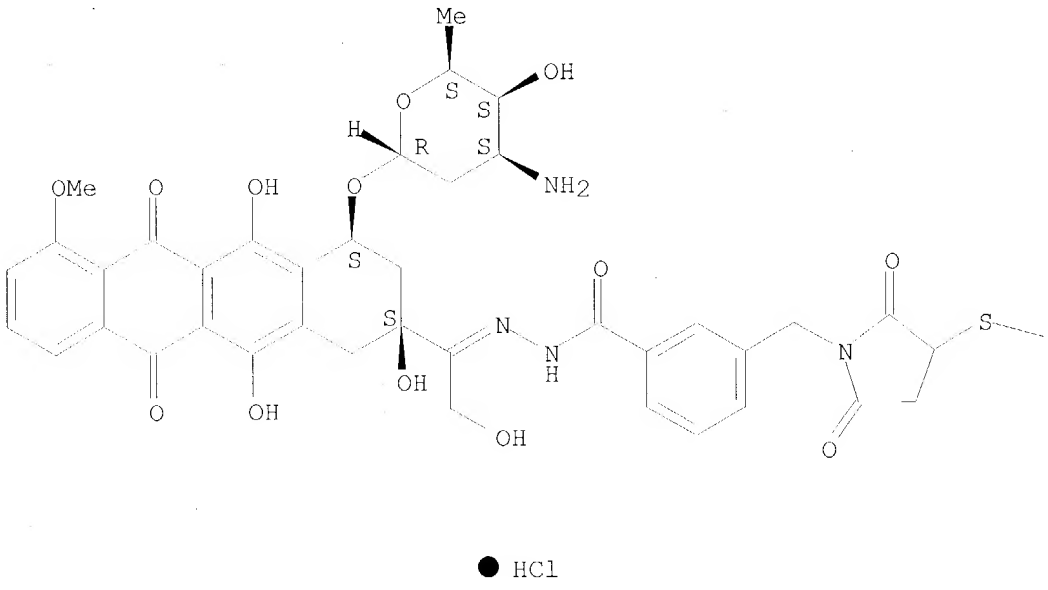
CRN 76-05-1
CMF C2 H F3 O2



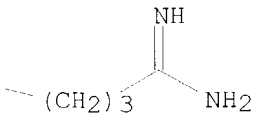
L3 ANSWER 2 OF 10 REGISTRY COPYRIGHT 2003 ACS
RN 342607-00-5 REGISTRY
CN Benzoic acid, 3-[[3-[(4-amino-4-iminobutyl)thio]-2,5-dioxo-1-pyrrolidinyl]methyl]-, [1-[(2S,4S)-4-[(3-amino-2,3,6-trideoxy-.alpha.-L-lyxo-hexopyranosyl)oxy]-1,2,3,4,6,11-hexahydro-2,5,12-trihydroxy-7-methoxy-6,11-dioxo-2-naphthacenyl]-2-hydroxyethylidene]hydrazide, monohydrochloride (9CI) (CA INDEX NAME)
FS STEREOSEARCH
MF C43 H48 N6 O13 S . Cl H
SR CA
LC STN Files: CA, CAPLUS, TOXCENTER

Absolute stereochemistry.
Double bond geometry unknown.

PAGE 1-A



● HCl



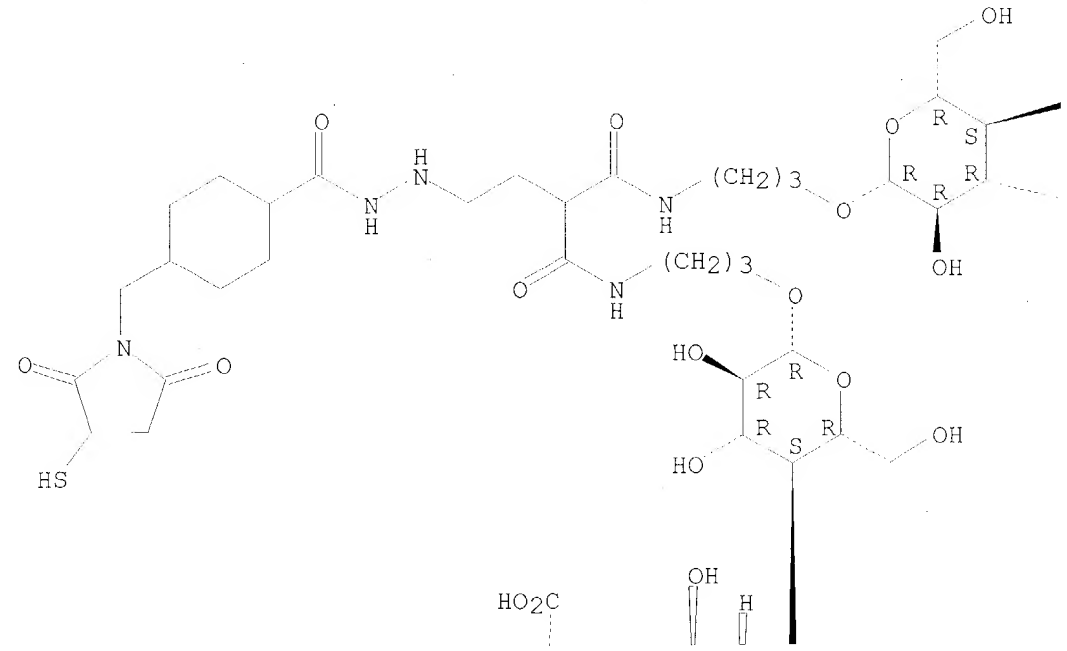
1 REFERENCES IN FILE CA (1957 TO DATE)
1 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA
1 REFERENCES IN FILE CAPLUS (1957 TO DATE)

REFERENCE 1: 135:13979

L3 ANSWER 3 OF 10 REGISTRY COPYRIGHT 2003 ACS
RN 274260-28-5 REGISTRY
CN Cyclohexanecarboxylic acid, 4-[(3-mercapto-2,5-dioxo-1-pyrrolidinyl)methyl]-, 2-[4-[[3-[[O-(N-acetyl-.alpha.-neuraminosyl)-(2.fwdarw.3)-O-.beta.-D-galactopyranosyl-(1.fwdarw.4)-.beta.-D-glucopyranosyl]oxy]propyl]amino]-3-[[[3-[[O-(N-acetyl-.alpha.-neuraminosyl)-(2.fwdarw.3)-O-.beta.-D-galactopyranosyl-(1.fwdarw.4)-.beta.-D-glucopyranosyl]oxy]propyl]amino]carbonyl]-4-oxobutyl]hydrazide (9CI) (CA INDEX NAME)
FS STEREOSEARCH
MF C69 H113 N7 O43 S
SR CA
LC STN Files: CA, CAPLUS, TOXCENTER

Absolute stereochemistry.

PAGE 1-A



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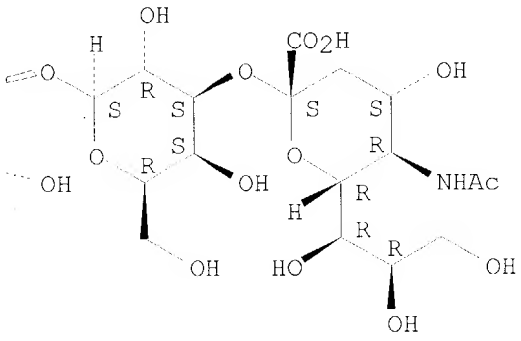

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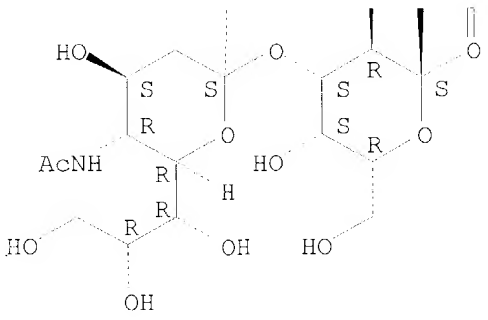


**PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT**

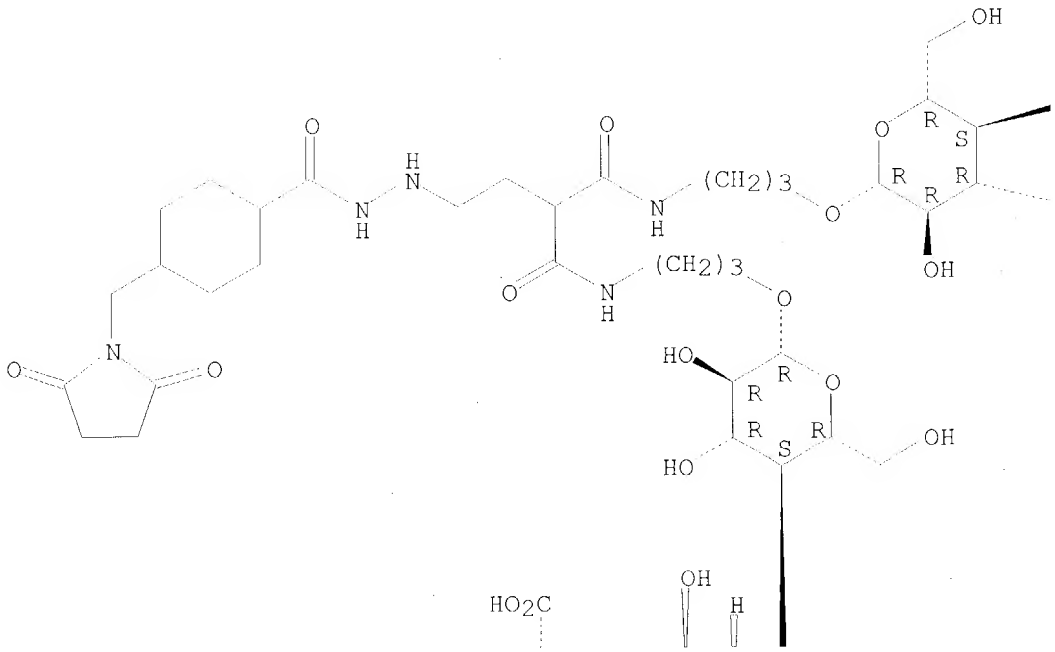
1 REFERENCES IN FILE CA (1957 TO DATE)
1 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA
1 REFERENCES IN FILE CAPLUS (1957 TO DATE)

REFERENCE 1: 133:43736

L3 ANSWER 4 OF 10 REGISTRY COPYRIGHT 2003 ACS
RN 274260-27-4 REGISTRY
CN Cyclohexanecarboxylic acid, 4-[(2,5-dioxo-1-pyrrolidinyl)methyl]-, 2-[4-[[3-[[O-(N-acetyl-.alpha.-neuraminosyl)-(2.fwdarw.3)-O-.beta.-D-galactopyranosyl-(1.fwdarw.4)-.beta.-D-glucopyranosyl]oxy]propyl]amino]-3-[[[3-[[O-(N-acetyl-.alpha.-neuraminosyl)-(2.fwdarw.3)-O-.beta.-D-galactopyranosyl-(1.fwdarw.4)-.beta.-D-glucopyranosyl]oxy]propyl]amino]carbonyl]-4-oxobutyl]hydrazide (9CI) (CA INDEX NAME)
FS STEREOSEARCH
MF C69 H113 N7 O43
SR CA
LC STN Files: CA, CAPLUS, TOXCENTER

Absolute stereochemistry.

PAGE 1-A



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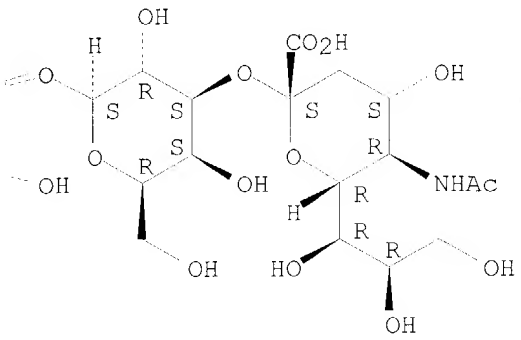

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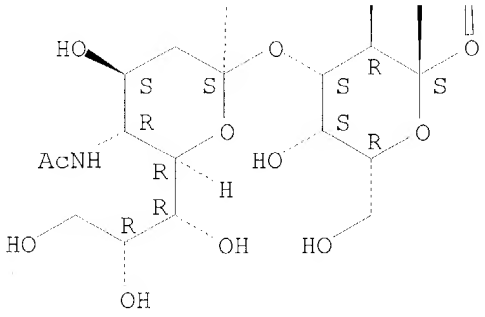

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1 REFERENCES IN FILE CA (1957 TO DATE)
1 REFERENCES IN FILE CAPLUS (1957 TO DATE)

REFERENCE 1: 133:43736

L3 ANSWER 5 OF 10 REGISTRY COPYRIGHT 2003 ACS
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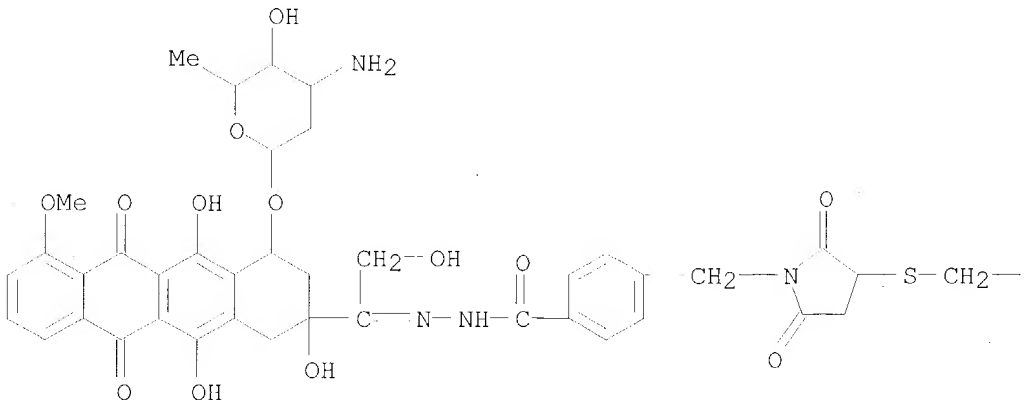
MF (C2 H4 O)n C88 H96 N10 O29 S2
CI PMS
PCT Polyether
SR CA
LC STN Files: CA, CAPLUS, TOXCENTER

PAGE 1-A



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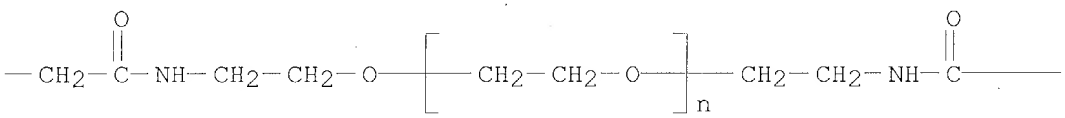

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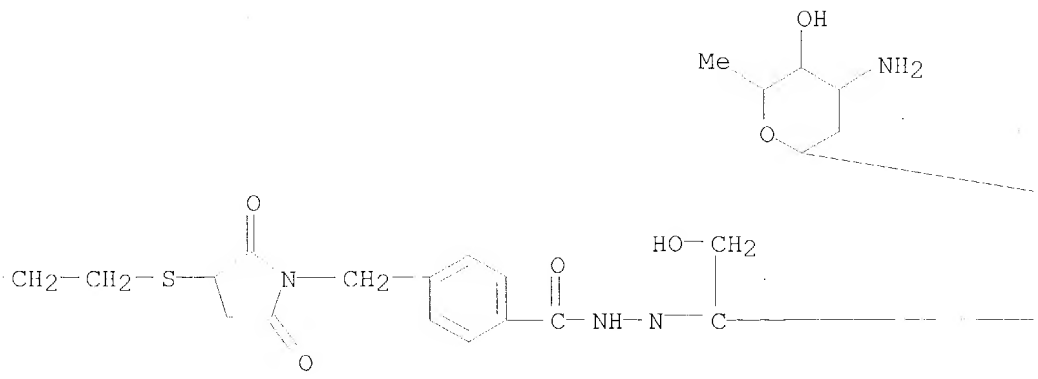

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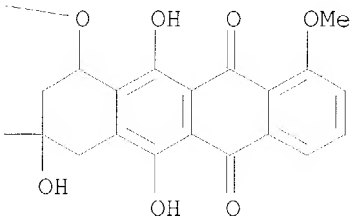

1 REFERENCES IN FILE CA (1957 TO DATE)
1 REFERENCES IN FILE CAPLUS (1957 TO DATE)

REFERENCE 1: 132:170955

L3 ANSWER 6 OF 10 REGISTRY COPYRIGHT 2003 ACS
RN 258844-02-9 REGISTRY
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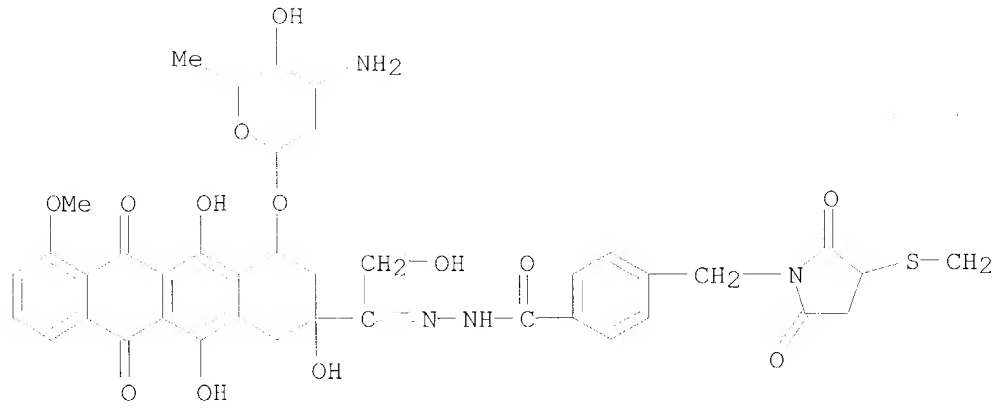
MF (C2 H4 O)n C45 H51 N5 O15 S
CI PMS
PCT Polyether
SR CA
LC STN Files: CA, CAPLUS, TOXCENTER

PAGE 1-A



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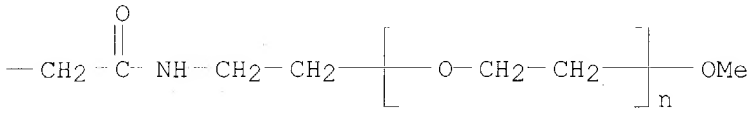


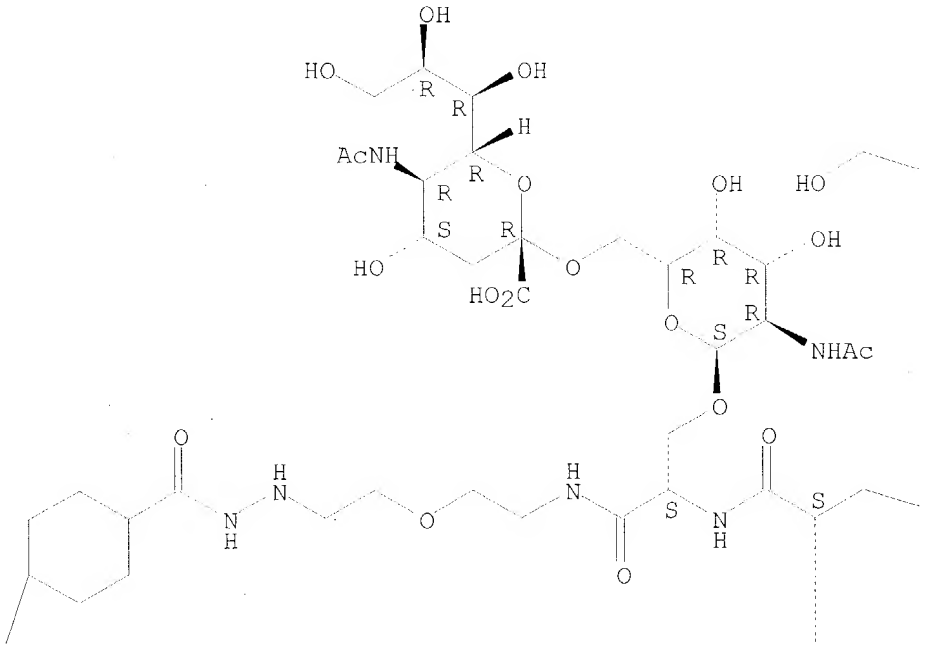
1 REFERENCES IN FILE CA (1957 TO DATE)
1 REFERENCES IN FILE CAPLUS (1957 TO DATE)

REFERENCE 1: 132:170955

L3 ANSWER 7 OF 10 REGISTRY COPYRIGHT 2003 ACS
RN 207503-53-5 REGISTRY
CN L-Serinamide, N-acetyl-O-[2-(acetylamino)-6-O-(N-acetyl-.alpha.-neuraminosyl)-2-deoxy-.alpha.-D-galactopyranosyl]-L-seryl-O-[2-(acetylamino)-6-O-(N-acetyl-.alpha.-neuraminosyl)-2-deoxy-.alpha.-D-galactopyranosyl]-L-seryl-O-[2-(acetylamino)-6-O-(N-acetyl-.alpha.-neuraminosyl)-2-deoxy-.alpha.-D-galactopyranosyl]-N-[2-[2-[2-[[4-[(2,5-dihydro-2,5-dioxo-1H-pyrrol-1-yl)methyl]cyclohexyl]carbonyl]hydrazino]ethoxy]ethyl]- (9CI) (CA INDEX NAME)
FS STEREOSEARCH
MF C84 H133 N13 O50
SR CA
LC STN Files: CA, CAPLUS, TOXCENTER

Absolute stereochemistry.

PAGE 1-A



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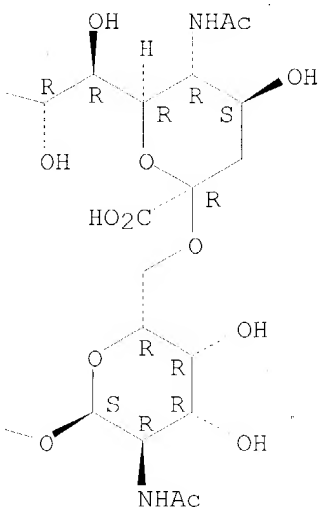


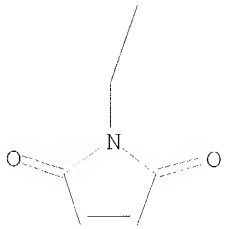


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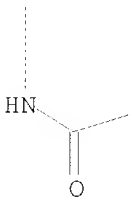


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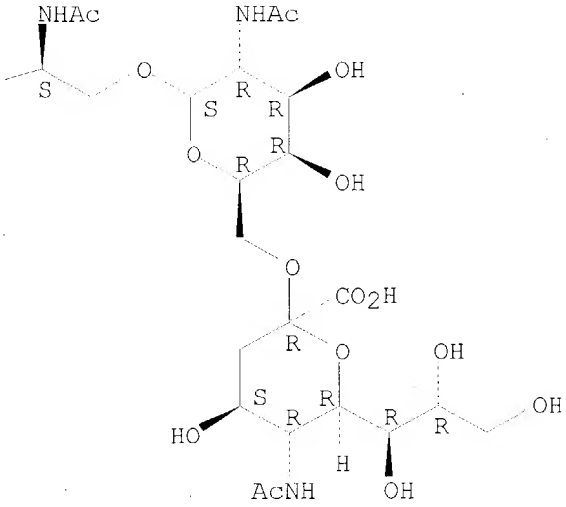

**PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT**

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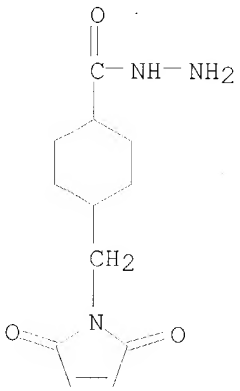
1 REFERENCES IN FILE CAPLUS (1957 TO DATE)

REFERENCE 1: 129:3682

L3 ANSWER 8 OF 10 REGISTRY COPYRIGHT 2003 ACS
RN 181148-00-5 REGISTRY
CN Cyclohexanecarboxylic acid, 4-[(2,5-dihydro-2,5-dioxo-1H-pyrrol-1-yl)methyl]-, hydrazide (9CI) (CA INDEX NAME)
FS 3D CONCORD
MF C12 H17 N3 O3
CI COM
SR CA
LC STN Files: CA, CAPLUS, TOXCENTER, USPATFULL



**PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT**

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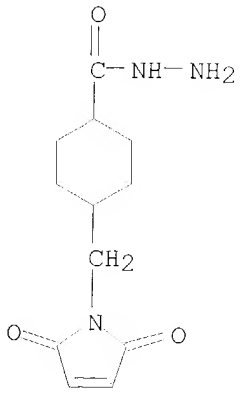
REFERENCE 1: 136:400166

REFERENCE 2: 131:143211

REFERENCE 3: 128:203897

REFERENCE 4: 125:189998

L3 ANSWER 9 OF 10 REGISTRY COPYRIGHT 2003 ACS
RN 174422-72-1 REGISTRY
CN Cyclohexanecarboxylic acid, 4-[(2,5-dihydro-2,5-dioxo-1H-pyrrol-1-yl)methyl]-, hydrazide, monohydrochloride (9CI) (CA INDEX NAME)
MF C12 H17 N3 O3 . Cl H
SR CA
LC STN Files: CA, CAPLUS, TOXCENTER, USPATFULL
CRN (181148-00-5)



● HCl

5 REFERENCES IN FILE CA (1957 TO DATE)
5 REFERENCES IN FILE CAPLUS (1957 TO DATE)

REFERENCE 1: 135:41770

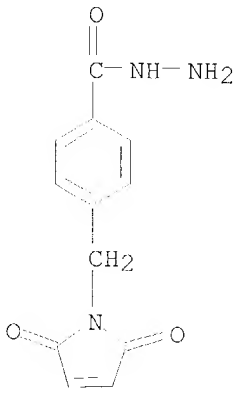
REFERENCE 2: 132:127703

REFERENCE 3: 129:3682

REFERENCE 4: 128:152804

REFERENCE 5: 124:212048

L3 ANSWER 10 OF 10 REGISTRY COPYRIGHT 2003 ACS
RN 129506-88-3 REGISTRY
CN Benzoic acid, 4-[(2,5-dihydro-2,5-dioxo-1H-pyrrol-1-yl)methyl]-, hydrazide (9CI) (CA INDEX NAME)
FS 3D CONCORD
MF C12 H11 N3 O3
SR CA
LC STN Files: CA, CAPLUS, TOXCENTER, USPATFULL



**PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT**

1 REFERENCES IN FILE CA (1957 TO DATE)
1 REFERENCES IN FILE CAPLUS (1957 TO DATE)

REFERENCE 1: 113:148405